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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/334,325	06/16/99	CEDERHOLM-WILLIAMS S	CV0276A

HM22/0728

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EXAMINER	
CHEN,S	
ART UNIT	**PAPER NUMBER**
1633	8

DATE MAILED: 07/28/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary

Application No.	Applicant(s)
09/334,325	Stewart Cederholm-Williams
Examiner	**Group Art Unit**
Shin-Lin Chen	1633

☒ Responsive to communication(s) filed on *May 8, 2000*

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-4 and 13-16* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-4 and 13-16* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

DETAILED ACTION

The amendment filed 5-8-00 has been entered. Claims 1-3 have been amended. Claims 13-16 have been added. Claims 5-12 have been canceled. Claims 1-4 and 13-16 are pending.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-4 remain rejected and claims 13-16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, and is repeated for the reasons set forth in the preceding Official action mailed 1-3-00 (Paper No. 5). The amendments have been fully considered and they are not found persuasive.

Claims 13-16 are directed to a method of transforming a cell with a fibrin gel entrapping a nucleic acid *in vitro* or *in vivo,* wherein the nucleic acid is a plasmid or is incorporated in a virus.

Applicants argue that the Office's rejection of claims 1 and 2 is for lack of utility, and applicants are not required to provide proofs that the present invention works. Applicants further argue that transformation of a cell was well known in the art and all the vectors described in the

many gene therapy articles cited in the specification and references will be effective in an appropriate context. This is not found persuasive because the claims read on transforming a cell with a fibrin gel entrapping a nucleic acid which would transform the cell. The rejection of the claims is not for the lack of utility but for the lack of enablement of the claimed invention. Although is was well known in the art to transform a cell with a nucleic acid *in vitro*, it is unclear whether a nucleic acid entrapped in a fibrin gel would be released into the cytoplasm of the cell and enters the nucleus for the expression of said nucleic acid once the fibrin gel is taken up by the cell. The specification of the present application only discloses the preparation of the fibrin gel and the preparation of the nucleic acid in a fibrin gel. The specification fails to demonstrate evidence that the fibrin gel entrapping the nucleic acid would be capable of transforming a cell *in vitro* or *in vivo*. Thus, the specification of the present application does not enable a method of transforming a cell with a fibrin gel entrapping a nucleic acid *in vitro* or *in vivo*.

Applicants argue that the rejection of claims 3 and 4 are also for lack of utility and the applicants is not claiming gene therapy but a tool for use in gene therapy. Applicants further argue that the literatures cited in the amendment shows that gene therapy is doable. This is not found persuasive because the state of the art in gene therapy was unpredictable at the time of the invention. The rejection of claims 3 and 4 is not for lack of utility but for lack of enablement. Claims 3 and 4 claim "a method of **conducting gene therapy**..." and therefore, read on a method of using cells adhered with fibrin gel containing nucleic acid for gene therapy for any disease or disorder *in vitro* and *in vivo*. Thus, the cells as set forth above are expected to provide

therapeutic effects for the gene therapy of any disease or disorder in an animal *in vitro* and *in vivo*.

Although applicants cited the literatures associated with gene therapy for various diseases, the state of the art in gene therapy was unpredictable at the time of the invention. Even the literature cited by the applicants (Exhibit a) indicates that there are problems with gene therapy. For example, exhibit a states a trial of gene therapy for cancer that "Overall, the trial was not a success, but one patient,..., astounded all the expectations....But, as Blease readily admits, this is not the whole answer because, of the other 14 patients, only one other showed any regression." In addition, in a trial of gene therapy for AIDS, "but the problem came with the expression of the gene, only three people show evidence of genetic marking" and "we never saw very high marking-only about one in a million cells". The type of nucleic acid is to be used for gene therapy for a specific disease or disorder, the vector used, the administration route of said vector or said nucleic acid, the immune response of the host, the efficiency of gene transfer and the expression of said nucleic acid *in vivo* are all important factors for a successful gene therapy for any particular disease or disorder. Therefore, in view of the unpredictability of gene therapy and the reasons set forth above, one skilled in the art at the time of the invention would require undue experimentation to practice the invention over the full scope claimed.

Applicants argue that the tool as filed in the present application can be used in the methods of fully successful gene therapies, and the invention can be practiced without undue experimentation. Applicants further argue that Exhibit E and Exhibit F indicate gene therapy can

be successful. This is not found persuasive because the results presented in Exhibits E and F only show that the use of a specific vector containing a specific gene for a particular disease could be successful in gene therapy, and the reasons as set forth above. Thus, claims 3 and 4 remain rejected under 35 U.S.C. 112 first paragraph for the reasons set forth above and the reasons set forth in the preceding Official action mailed 1-3-00 (Paper No. 5).

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 3 and 4 remain rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: whether the implanted transformed cells are present long enough to secret therapeutic effective amount of therapeutic product into the implanted site to exhibit therapeutic effect on the subject.

Applicants argue that there is no ambiguity in claims 3 and 4. This is not found persuasive because claims 3 and 4 are rejected due to being incomplete method for omitting essential steps. The method claimed is not complete because it is unclear whether the implanted transformed cells could provide therapeutic effects to the subject.

Conclusion

No claim is allowed.

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (703) 305-1678. The examiner can normally be reached on Monday to Friday from 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on (703) 308-0447. The fax phone number for this group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

Shin-Lin Chen, Ph.D.

DEBORAH J.R. CLARK
PRIMARY EXAMINER